(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 31 March 2005 (31.03.2005)

PCT

(10) International Publication Number WO 2005/028444 A1

- (51) International Patent Classification⁷: C07D 217/22, 401/04, 405/04, 405/14, 401/14, 413/14, 409/14, 413/04, 413/10, 417/14, A61K 31/4725, A61P 35/00
- 46 Center Grove Road, Apt U-414, Randolph, NJ 07869 (US). KIM, Sunkyu [US/US]; 10 Suffolk Street, #5, Cambridge, MA 02139 (US).
- (21) International Application Number:
 - PCT/EP2004/010688
- (74) Agent: GRUBB, Philip; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).
- (22) International Filing Date:
 23 September 2004 (23.09.2004)
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/505,457

24 September 2003 (24.09.2003) US

- (71) Applicant (for all designated States except AT, US): NO-VARTIS AG [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).
- (71) Applicant (for AT only): NOVARTIS PHARMA GMBH [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): FINK, Cynthia, Anne [US/US]; 1 Kensington Court, Lebanon, NJ 08833 (US). PEREZ, Lawrence, Blas [US/US]; 5 Meadowland Drive, Hopkinton, MA 01748 (US). RAMSEY, Timothy, Michael [US/US]; 45 Ox Bow Road, Weston, MA 02493 (US). YUSUFF, Naeem [US/US]; 8 Watson Street, Cambridge, MA 02139 (US). VERSACE, Richard, William [US/US]; 69 Townsend Road, Wanaque, NJ 07465 (US). BATT, David, Bryant [US/US]; 33 Campbell Road, Wayland, MA 01778 (US). SABIO, Michael, Lloyd [US/US];
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

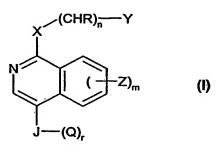
Published:

ZW.

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 1,4-DISUBSTITUTED ISOQUINILONE DERIVATIVES AS RAF-KINASE INHIBITORS USEFUL FOR THE TREATMENT OF PROLIFERATIVE DISEASES



(57) Abstract: This invention relates to compounds of formula (I) wherein the variable substituents are described herein. The compounds are useful for the treatment of conditions and diseases characterized by an aberrant MAP kinase signaling pathway, such as cancer.